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EXAMINER	
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SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/18/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/380,337	CHANDRASEKHARAPPA ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,19-24,26,30 and 32-37* is/are pending in the application.

4a) Of the above claim(s) *34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 19-24, 26, 30, 32, 36-37* is/are rejected.

7)☒ Claim(s) *3,4 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Appeal Brief filed September 8, 2006 in response to the Office Action of February 24, 2005 is acknowledged and has been entered. Upon review and reconsideration in and order to clarify issues for presentation to the Board, the finality of the previous final office action is hereby withdrawn. Claims 1, 3-5, 19-24, 26, 30, 32-33, 36-37 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC 112

3. Claims 1, 5, 30, 33, 36, 37 are rejected under 35 USC 112, first paragraph because the specification, while enabling for an isolated or recombinant nucleic acid comprising SEQ ID NO:1/ SEQ ID NO:3, does not reasonably provide enablement for an isolated or recombinant nucleic acid encoding menin, SEQ ID NO:2, isolated or recombinant nucleic acid encoding a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to an isolated or recombinant nucleic acid encoding menin, SEQ ID NO:2, isolated nucleic acid that encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2. This means that the claims are drawn to a whole universe of nucleic acid molecules including any degenerate nucleic acid molecule that encodes any polypeptide with at least 95% identity to SEQ ID NO:2, wherein the differences in the encoded protein can occur at any site and in any one of 31 of the 610 amino acids of SEQ ID NO:2.

The specification teaches that the invention relates to the discovery of a novel tumor suppressor gene which is associated with multiple endocrine neoplasia type 1 (p. 1, lines 1-2), SEQ ID NO:3 (p. 2 line 27). The specification further teaches that the lack of a functional menin polypeptide, either by absence of the protein, its alteration and/or associated mutations in the corresponding gene have been identified in individuals with the familial multiple endocrine neoplasia type I. The specification teaches that the invention is the discovery that the presence of mutations in the gene designated Men1 are associated with individuals that are at risk for sporadic cancers (p. 15, lines 5-12). Sequence of DNA from MEN-1 affected individuals allowed identification of both wild-type MEN1 allele and many mutated forms of MEN1. The mutated gene can be the result of a variety of different frameshift, nonsense, missense and/or in-frame deletion mutations wherein analysis of mutated forms of MEN1 isolated from affected individuals are summarized in Figures 3-4 (p. 15, lines 13-17). The identification of the MEN1 gene provides a new window into the mechanism of endocrine tumorigenesis, facilitates accurate early diagnosis of MEN1 associated cancers and provides preclinical identification of individuals with FMEN1 symdrome (p. 15, lines 22-26). The specification summarizes mutations identified in 15 unrelated MEN1 patients wherein different missense, frameshift and nonsense mutations are identified in each of exons 2-10 (p. 3, lines 4-14 and Figures 3-4). The specification specifically states that different patients suffering from multiple endocrine neoplasia type 1 have different mutations in their MEN1 gene (p. 33, lines 4-5). The specification states that of the mutations encountered, two mutations were encountered twice (p. 3, lines19-21) in two families not known to be related (p. 53, lines 2-3) and that different patients suffering from MEN1 have

different mutations in their MEN1 gene (p. 33, lines 3-4) although being inheritable, affected kindreds tend to present with the same mutations (p. 52, lines 27-32).

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

One cannot extrapolate the teaching of the specification to the scope of the claims because one would not know how to use the broadly claimed nucleic acid molecules. The claims read on a whole universe of undefined molecules which encode a polypeptide with 95% identity to SEQ ID NO:2. However, the specification teaches that the invention is the novel discovery that the presence of mutations in the gene designated MEN1, SEQ ID NO:3, are associated with

individuals that are at risk for sporadic cancers and that the identification of MEN1 as a marker for FMEN1 has diagnostic uses in cancer and endocrine disease. Thus, it appears that the only use contemplated for the novel MEN1 nucleic acid is as a diagnostic identifier of patients. However, the specification teaches that different patients suffering from MEN1 have different mutations in their MEN1 gene and that these mutations are located throughout exons 2 through 10 of the gene and it appears that at the time the invention was made there was not an identification of specific residues critical to the diagnostic function of the claimed invention. Given the different mutations in the different exons, given the teaching that different patients present different mutations in their MEN1 genes, it is clear that one would not be able to predictably distinguish between those nucleic acids that encode amino acid sequences having at least 95% identity to SEQ ID NO:2 that would be useful for diagnostic identification of patients from those that would not. In the absence of the ability to distinguish, one would not know how to use the claimed invention. Further, given the different mutations in the MEN1 genes, it is also clear that one would not be able to predictably distinguish between those encoded proteins with 95% identity to SEQ ID NO:2 that were the result of mutations associated with risk for sporadic cancers from those that are not. Given that the function of the encoded protein was unknown at the time the invention was made, as disclosed by Agarwal et al (Human Molecular Genetics, 1997, 6:1169-1175) published after the filing of the priority document, who specifically teach that there is no information about function and three dimensional structure of menin (p. 1173, col 1), one would not know how to use polypeptides with 95% identity to SEQ ID NO:2 that were not the result of mutations associated with risk for sporadic cancers.

Further, as drawn to the whole universe of degenerate nucleic acids, the specification has clearly identified only a single nucleic acid that encodes SEQ ID NO:2, SEQ ID NO:3 and the cDNA, SEQ ID NO:1, wherein that single sequence has been identified to be mutated and therefore useful as a diagnostic for individuals with the familial multiple endocrine neoplasia type. However, neither the specification nor the art of record provides a nexus between any other sequence encoding SEQ ID NO:2 and a nucleic acid useful for said diagnositic. Although the specification also provides information drawn to mutations of SEQ ID NO:3, this does not permit an extrapolation of the information drawn to SEQ ID NO:3 to any other nucleic acid encoding SEQ ID NO:2. Further, it is noted that Wautot (Human Mutation, 2002, 20:35-47, published five years post-priority date of the instant application) specifically teaches that "**the** (emphasis added) MEN1 gene was identified in 1997 wherein genomic analysis of tumoral DNA in MEN1 patients showed loss of the wild-type MEN1 allele inherited from the unaffected parent (p. 36, col 1). Although the references gives a detailed history of the progression of research of the germline mutation profile of MEN1 in multiple endocrine neoplasia type 1 and specifically discusses relevant research findings drawn to mutations, as well as the structure and function of the encoded protein, there is neither a suggestion nor guidance on any mutated nucleic acid, other than the one identified by the instant inventors (SEQ ID NO:3/1), that encodes SEQ ID NO:2 that is associated in any way with multiple endocrine neoplasia type 1. Certainly given the known degeneracy of the genetic code, it cannot be predicted which, if any other nucleic acid encoding SEQ ID NO:2 is associated with a germline mutation profile multiple endocrine neoplasia type 1.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to use the claimed nucleic acids which encode a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

Some of Applicant's arguments, recited in the Appeal Brief, drawn to the previous rejection of claims 1, 30, 32-33, 36-37 in the Action mailed February 24, 2005, Section 4, pages 2-3 are relevant to the instant rejection.

Applicant argues that the specification provides ample guidance for making and using the claimed sequences and the practitioner could reasonably expect to be able to successfully identify sequences that fall within the scope of the invention and use them in accordance with the disclosure because the function of the encoded protein is known because (1) page 1, lines 1-3 discloses that menin polypeptide plays a role in neoplastic disease (2) applicants have shown numerous mutations in all of the MEN1 coding exons that lead to nonfunctional MEN1 alleles in patients having multiple endocrine neoplasia type 1.

The arguments have been considered but have not been found persuasive because (1') although one could reasonably expect to be able to successfully identify sequences that fall within the scope of the invention, for the reasons set forth above, one would not know how to use them in accordance with the disclosure because contrary to Applicant's arguments, the function of the menin polypeptide was not known at the time the invention was made, as clearly set forth in Agarwal et al, *Supra*, in a post priority date filing, and even if that function had

been known, the specification provides no information drawn to amino acids critical to that function in order to provide guidance to one of skill for how to use an encoded polypeptide with at least 95% identity to SEQ ID NO:2. In addition, it is noted that Applicant is arguing limitations not recited in the claims as currently constituted. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Guens , 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

(2') although Applicant has shown numerous mutations in all of the MEN1 coding exons of SEQ ID NO:3 that lead to nonfunctional MEN1 alleles in patients having multiple endocrine neoplasia type 1, this teaching has not enabled the broadly claimed invention because (a) the claims are not limited to mutations in SEQ ID NO:3 and even if they were limited to mutations in SEQ ID NO:3, given the differences in the patients presenting with mutations, given the differences in the exons mutated, one could not predictably distinguish between those sequences which are associated with mutations in patient having multiple endocrine neoplasia type 1 and those that are not. In addition, no nexus has been provided between SEQ ID NO:3 and any of the whole universe of encoding nucleic acids claimed, thus, one could not predictably identify which nucleic acids, other than SEQ ID NO:3 which encode SEQ ID NO:2 would be mutated and if mutated, which of those mutated nucleic acids would be associated with patients having multiple endocrine neoplasia type 1. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Guens , 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that although the claimed genus encompasses a large number of nucleic acids, the specification provides guidance such that one of skill in the art could identify any one of the claimed nucleic acids that fall within the scope of the claims, wherein the practitioner could readily use manual or computer sequence alignments using SEQ ID NO:2 as a structural reference point to determine whether nucleic acid sequences have the specified identities. The argument has been considered but has not been found persuasive because the although one could readily identify sequences with at least 95% identity to SEQ ID NO:2, and by extension, nucleic acids encoding said sequences, for the reasons set forth above, one would not know how to predictably use those sequences.

Applicant reiterates arguments drawn to the level skill in the art wherein one could readily identify a polynucleotide with at least 95% identity to a polynucleotide encoding SEQ ID NO:2 and points to Guru et al, of record who teach an amino acid sequence encoded by the mouse gene having 97% identity to human menin. The argument has been considered but has not been found persuasive because the although one could readily identify sequences with at least 95% identity to SEQ ID NO:2, and by extension, nucleic acids encoding said sequences, for the reasons set forth above, one would not know how to predictably use those sequences.

Applicant argues that given the identification of the role of the encoded protein in neoplastic disease such as the syndrome multiple endocrine neoplasia type 1, one would know how to use the claimed invention. The argument has been considered but has not been found persuasive because, as set forth above, the function of the menin polypeptide was not known at the time the invention was made, as clearly set forth in Agarwal et al, *Supra*.

Applicant further argues that the specification teaches that the nucleic acid sequences of the invention can be used in methods such as detecting the presence or absence of a MEN1 gene in a patient or relative thereof. The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted, the claims are not drawn to specifically identified mutations that would be expected to be found within a kindred. In point of fact, the specification makes clear that different kindreds present with different mutational patterns and the broad claims are not enabled because one could not predictably identify those nucleic acids encoding a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 that would function as suggested.

Applicant argues that the Examiner provides no reasoning or evidence as to why one of skill could not reasonably expect the highly homologous structures as claimed to function similarly. The argument has been considered but has not been found persuasive because the claims are not drawn to any particular function. Further, even if they were drawn to a function, it is clear from the teaching of Agarwal et al, *Supra* that the function of the encoded protein was unknown at the time the invention was made. Further, it is clear that, at the time the invention was made, the finding of a mutation in one patient/kindred was not predictive of the finding of the same mutation in another.

Applicant states that claims 36 and 37 are enabled and reiterates the argument that one could readily identify nucleic acids that encode variants of the exemplary menin protein. The argument has been considered previously and not found to be persuasive .

Applicant argues that the claimed variants could be used to express menin proteins in order to make antibodies. The argument has been considered but has not been found persuasive because for the reasons set forth above, no nucleic acid other than SEQ ID NO:3/1 that have been mutated can be predictably identified.

Further, some of Applicant's arguments drawn to the rejection of claims 1, 3-5, 19-24, 26, 30, 32-33, 36-37 in the paper mailed February 24, 2005, Section 5, pages 3-4 are relevant to the instant rejection

Applicant argues that the claims at issue are not directed to menin proteins and that the menin gene has been shown to be mutated in patients with endocrine neoplasia and states that because the gene is mutated, the encoded protein has a function. The argument has been considered but has not been found persuasive because as set forth above, at the time the invention was made, function of the encoded protein was unknown. Further, even if the encoded protein were to have a function representing the end product of a mutated gene, for the reasons set forth above, one could not predictably identify those nucleic acids encoding SEQ ID NO:2, other than SEQ ID NO:3/1 that are useful for diagnostic identification as disclosed in the specification.

Applicant argues that since SEQ ID NO:3 has been shown to be mutated in patients, that the claimed sequences therefore have demonstrated biological function. The argument has been considered but has not been found persuasive because although SEQ ID NO:3 and SEQ ID NO:1 both have demonstrated biological function, this function cannot be correlated to the function of any other nucleic acid encoding SEQ ID NO:2.

Applicant argues that the cited art does not provide any evidence that defects in MEN1 genes are not believed to underlie the disease multiple endocrine type 1

neoplasia. The argument has been considered but has not been found persuasive, as it is not clear why Applicant makes this argument. In particular, it is noted that claims drawn specifically to SEQ ID NO:1 and SEQ ID NO:3 are not herein rejected.

Given that MEN1 gene was identified by Wautot et al as the responsible gene for multiple endocrine type 1 neoplasia, one of skill could use antibodies to examine menin levels in patients with the disease to further characterize the disease in any individual patient. The argument has been considered but has not been found persuasive because for the reasons set forth above, no nucleic acid other than SEQ ID NO:3/1 that have been mutated can be predictably identified.

Applicant reiterates arguments set forth above, that is that the nucleic acids could be used for diagnostic purposes. The argument has been considered but has not been found persuasive because the claims are not limited to SEQ ID NO:1 or SEQ ID NO:3 and for the reasons set forth above, one would not know how to use the claimed invention.

Applicant reiterates arguments set forth above, that is that the expression cassettes and vectors can be used as probes. The argument has been considered but has not been found persuasive because the claims are not limited to SEQ ID NO:1 or SEQ ID NO:3 and for the reasons set forth above, one would not know how to use the claimed invention.

4. Claims 1, 5, 30, 33, 36, 37 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 1, 5, 30, 33, 36, 37 are drawn to an isolated or recombinant nucleic acid encoding menin SEQ ID NO:2, isolated nucleic acid that encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2.

The specification teaches that the invention is the discovery that the presence of mutations in the gene designated Men1 are associated with individuals that are at risk for sporadic cancers (p. 15, lines 5-12). Sequence of DNA from MEN-1 affected individuals allowed identification of both wild-type MEN1 allele and many different mutated forms of said MEN1 wild-type allele. The mutated gene can be the result of a variety of different frameshift, nonsense, missense and/or in-frame deletion mutations wherein analysis of mutated forms of MEN1 isolated from affected individuals are summarized in Figures 3-4 (p. 15, lines 13-17). The specification teaches that unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conserved modified variants thereof, e.g. degenerate codon substitutions) and complementary sequences as well as the sequence explicitly indicated. However, it is noted that there is no indication that any sequence other than SEQ ID NO:3 which encodes SEQ ID NO:2 was found to be mutated.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the

> genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of an isolated or recombinant nucleic encoding menin, wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2, per Lilly by structurally describing a representative number of isolated or recombinant nucleic encoding menin, wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the isolated or recombinant nucleic encoding menin, wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 in a manner that satisfies either the Lilly or Enzo standards. Although the specification describes SEQ ID NO:1 as well as mutated genes associated with individuals that are at risk for sporadic cancers, that is variants of SEQ ID NO:3 (see Figures 3 and 4), wherein said mutations comprise a variety of different frameshift, nonsense, missense and/or in-frame deletion mutations throughout the 10 exons of the gene, no consistent pattern of mutations has been disclosed. The specification does not provide the complete structure of any isolated or recombinant nucleic acid encoding menin, wherein said nucleic acid encodes a protein comprising an amino

acid sequence having at least 95% identity to SEQ ID NO:2 other than the cited nucleic acids, nor does the specification provide any partial structure of such isolated or recombinant nucleic acid encoding menin, wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 coupled with a known or disclosed correlation between structure and function. Although the specification discloses as set forth above, this does not provide a description of isolated or recombinant nucleic acid encoding menin, wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 would satisfy the standard set out in Enzo.

The specification also fails to describe the isolated or recombinant nucleic acid encoding menin, wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 by the test set out in Lilly. The specification describes only SEQ ID Nos 1 and 3 and the unrelated mutated SEQ ID NO:3 sequences. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the isolated or recombinant nucleic acid encoding menin, wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 that is required to practice the claimed invention.

Some of Applicant's arguments drawn to the previous rejection of claims 1, 30, 33, 36, 37 are relevant to the instant rejection.

Applicant reiterates case law drawn to written description.

Applicant reiterates arguments drawn to a known biological role of the protein. The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted. Further, as set forth above, the function of the encoded protein was unknown at the time the invention was made, as disclosed by Agarwal et al, *Supra*. Further, no nexus has been established between any structure and any particular function, structural features common to the members of the genus, which features constitute a substantial portion of the genus are not taught and the claims do not meet the requirements for written description under 35 USC 112, first paragraph.

Applicant argues that numerous mutations that lead to nonfunctional MEN1 alleles are taught. The argument has been considered but has not been found persuasive because although numerous mutations that lead to nonfunctional MEN1 alleles are taught, none of those specific mutations are drawn to structural features common to the members of the genus, which features constitute a substantial portion of the genus. The single example of mutated SEQ ID NO:3 does not provide for a written description of the claimed invention for the reasons set forth above. Finally, Applicant is arguing limitations not recited in the claims as currently constituted. The claims are drawn to a whole universe of undefined nucleic acid molecules and is not limited to MEN1 alleles mutated in patients presenting with disease multiple endocrine neoplasia type I. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Guens , 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the claims are drawn to a genus of compositions that are highly homologous nucleic acids that encode proteins comprising an amino

acid sequence having at least 95% identity to SEQ ID NO:2 and thus in contrast to Lilly, the claims provide a structural hallmark and cites the teaching in Lilly that in claims involving chemical materials, generic formulae usually indicate with a specificity what the generic claims encompasses and one could readily distinguish such a formula from others and thus one of skill can identify the species encompassed by the claims. The argument has been considered but has not been found persuasive because Applicant is mischaracterizing the teaching of the Court wherein the Court required that the written description requirement could be satisfied by structurally describing a representative number of isolated or recombinant nucleic acids or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." However, the instant specification provides no information drawn to structural features common to the members of the genus which features constitute a substantial portion of the genus and given the whole universe of molecules encompassed within the claimed invention, as well as the different and varied mutations found in patients with mutated MEN1 gene, it is clear that the exemplified nucleic acids are not a representative number of the isolated or recombinant nucleic acids.

Applicant argues that a structural hallmark is set out in the claims, that is the reference sequence is SEQ ID NO:2 and further argues that there is a correlation between this structural characteristic and a function. Applicant reiterates arguments drawn the demonstrated mutations in nucleic acids encoding SEQ ID NO:2 that can lead to a disease, multiple endocrine neoplasia type 1. The argument has been considered above but has not been found persuasive for the reasons set forth above.

Applicant reiterates arguments drawn to structural properties that identify the species within the genus that have been identified, that is nucleic acids that encode variants of SEQ ID NO:2. Applicant argues that the disclosure of multiple species in conjunction with the structural characteristics set forth in the claims is properly supports the description in the specification. The argument has been considered but has not been found persuasive for the reasons set forth above.

Applicant argues that claims 32 and 33 are properly supported and that claims 32-33 recite particular SEQ ID NOS that are disclosed in the specification, thus the claims are fully described. The argument has been considered but has not been found persuasive because claim 33 is not drawn to SEQ ID NOS 1 and 3 but rather is drawn to a transfected cell wherein the cell comprises a heterologous nucleic acid of claim 1. Applicant is reminded that claim 1 is drawn to an isolated or recombinant nucleic acid encoding a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2.

Applicant argues, as drawn to the previous rejection of claims 19-24 and 26 as lacking written description because the specification does not provide a written description of any recombinant nucleic acid encoding SEQ ID NO:2 other than SEQ ID NOS 1 and 3 that are mutated in patients with multiple endocrine neoplasia type 1, Applicant has disclosed a wildtype MEN1 allele and many mutated forms of MEN 1, wherein mutations occur in all of the coding exons. Further, Applicants have provided exemplary primers and probes that can be used to detect mutant and normal MEN1 alleles. The argument has been considered but has not been found persuasive because the specification provides information drawn only to genomic SEQ ID NO:3 and the cDNA from SEQ ID NO:3, SEQ ID

NO:1. Further, all of the exemplary primers and probes are specific to SEQ ID NO:1.

Applicant reiterates arguments drawn to a structural hallmark, the reference sequence, SEQ ID NO:2 and cites MEPE (2163 III)(a)(ii) which states that in the molecular biology arts, if an applicant discloses an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequence that encoded the amino acid sequence. The argument drawn to the structural hallmark has been considered but has not been found persuasive for the reasons set forth above. Further, the claims are not drawn to nucleic acid encoding SEQ ID NO:2, but rather are drawn to nucleic acid encoding a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2.

The arguments have been considered but have not been found persuasive for the reasons set forth above.

5. Claims 19-24 and 26 are rejected under 35 USC 112, first paragraph because the specification, while enabling for a method of determining the presence or absence of the MEN 1 gene, SEQ ID NO:3, does not reasonably provide enablement for a method of detecting the presence or absence of a mutation in a human MEN1 gene comprising contacting the sample with a first oligonucleotide that distinguishes between a wild type gene and a mutant form. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are drawn to a method of detecting the presence or absence of a mutation in a human MEN1 gene comprising contacting the sample with a first oligonucleotide that distinguishes between a wild type gene and a mutant form.

This means detecting any mutation with an oligonucleotide that distinguishes between a wild-type and a mutant form.

The specification teaches that the invention is the discovery that the presence of mutations in the gene designated Men1 are associated with individuals that are at risk for sporadic cancers (p. 15, lines 5-12). Sequence of DNA from MEN-1 affected individuals allowed identification of both wild-type MEN1 allele and many mutated forms of MEN1. The mutated gene can be the result of a variety of different frameshift, nonsense, missense and/or in-frame deletion mutations wherein analysis of mutated forms of MEN1 isolated from affected individuals are summarized in Figures 3-4 (p. 15, lines 13-17). The specification teaches that probes for the menin gene can be generated from the MEN1 sequences and discloses exemplary probes, all from SEQ ID NO:1, in Table 1, page 18. Further, the invention is also the discovery that different patients suffering from MEN1 have different mutations in their MEN1 gene (p. 33, lines 1-5). The specification teaches identification of mutations by a combination of PCR primer reactions using the primers described in Table 1 and dideoxyfingerprinting (p. 50, lines 22-30).

One cannot extrapolate the teaching of the specification to the scope of the claims because the specification provides no guidance on how to predictably identify a probe that distinguishes between the wild-type gene and a mutant form. This is clearly the critical feature of this invention. However, although the specification provides information drawn specifically to probes that bind to wild-type SEQ ID NO:1/3 the specification provides no information on probes that will specifically distinguish between wild-types and mutant forms of the gene. Given that the specification also teaches the wide variety of mutations found, given the finding that there are different patients suffering from MEN1 have different

mutations in their MEN1 gene, one would not know how to make probes that will distinguish between the wild-types and mutant forms of the gene that will function as claimed.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to use the claimed invention with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

6. Claims 19-24, 26 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 19-24, 26 are drawn to a method for detecting in a test sample the presence or absence of a mutation in a human MEN1 gene comprising a nucleotide sequence that encodes human menin as set forth in SEQ ID NO:2 comprising contacting said test sample with a first oligonucleotide having a sequence that discriminates between a wild-type gene and the mutant form of the gene and detecting the formation of a duplex between the gene and the first oligonucleotide sequence. The specification teaches that the invention is the discovery that the presence of mutations in the gene designated Men1 are associated with individuals that are at risk for sporadic cancers (p. 15, lines 5-12). Sequence of DNA from MEN-1 affected individuals allowed identification of both wild-type MEN1 allele and many mutated forms of MEN1. The mutated gene can be the result of a variety of different frameshift, nonsense, missense and/or in-frame deletion mutations wherein analysis of mutated forms of MEN1 isolated from affected individuals are summarized in Figures 3-4 (p. 15, lines 13-17). The specification

teaches that probes for the menin gene can be generated from the MEN1 sequences and discloses exemplary probes, all from SEQ ID NO:1, in Table 1, page 18. Further, the invention is also the discovery that different patients suffering from MEN1 have different mutations in their MEN1 gene (p. 33, lines 1-5). The specification teaches identification of mutations by a combination of PCR primer reactions using the primers described in Table 1 and dideoxyfingerprinting (p. 50, lines 22-30).

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of oligonucleotide having a sequence that discriminates between a wild-type

menin gene and the mutant form, per Lilly by structurally describing a representative number of oligonucleotides having a sequence that discriminates between a wild-type menin gene and the mutant form or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe oligonucleotides having a sequence that discriminates between a wild-type menin gene and the mutant form in a manner that satisfies either the Lilly or Enzo standards. Although the specification describes oligonucleotide that bind to wild-type menin gene, SEQ ID NO:1, no oligonucleotides that discriminate between wild-type menin gene and the mutant form have been disclosed. The specification does not provide the complete structure of any oligonucleotide having a sequence that discriminates between a wild-type menin gene and the mutant form, nor does the specification provide any partial structure of such oligonucleotide having a sequence that discriminates between a wild-type menin gene and the mutant form coupled with a known or disclosed correlation between structure and function. Although the specification discloses as set forth above, this does not provide a description of oligonucleotide having a sequence that discriminates between a wild-type menin gene and the mutant form would satisfy the standard set out in Enzo.

The specification also fails to describe oligonucleotide having a sequence that discriminates between a wild-type menin gene and the mutant form by the test

set out in Lilly. The specification describes only probes derived from SEQ ID NO:1. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the oligonucleotides having a sequence that discriminates between a wild-type menin gene and the mutant form that is required to practice the claimed invention. Since the specification fails to adequately describe the product critical to the claimed method and kit, it also fails to adequately describe the claimed method and kit.

7. Claims 19-24 and 26 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 19-24 and 26 are drawn to a method for detecting the presence or absence of a mutation in a human MEN1 gene that encodes human menin as set forth in SEQ ID NO:2. The assay, as contemplated in the specification is drawn to the identification of mutations in a human MEN1 gene that are associated with multiple endocrine neoplasia type 1. Thus, the claimed assay as broadly read, reads on the detection for the purpose of identifying subjects with multiple endocrine neoplasia type 1 mutations. The specification teaches a single genomic sequence, SEQ ID NO:3 that encodes human menin as set forth in SEQ ID NO:2 that is mutated and whose mutation is associated with multiple endocrine neoplasia type 1.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo

Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of the nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, per Lilly by structurally describing a representative number of nucleic acids encoding a human menin, SEQ ID NO:2 which is mutated, or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, nor does the specification provide any partial structure of such nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, nor any physical or chemical characteristics of the nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, nor any functional characteristics coupled with a known or disclosed correlation between structure and function other than SEQ ID NO:3. Although the specification discloses a single nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, this does not provide a description of nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, that would satisfy the standard set out in Enzo.

The specification also fails to describe the nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated, by the test set out in Lilly. The specification describes only a single nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated,. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the nucleic acid encoding a human menin, SEQ ID NO:2 which is mutated that is required to practice the claimed invention. Since the specification fails to adequately describe the product critical to the instant invention, it also fails to adequately describe the claimed method.

Some of Applicant's arguments drawn to the rejection of claims 19-24 and 26 in the Action mailed 2/24/05, page Section 8, page 7-8 are relevant to the instant rejection.

Applicant argues that wild-type MEN1 allele and many mutated forms of MEN 1 have been disclosed and Applicants have provided exemplary primers and probes that can be used to detect mutant and normal MEN1 alleles. The argument has been considered but has not been found persuasive because the disclosure of the single mutated SEQ ID NO:3 does not provide a written description for the broadly claimed invention.

Applicant argues that Applicant's recite a structural hallmark, the reference sequence, SEQ ID NO:2 and cites the MPEP that states that "if an amino acid sequence is disclosed, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encode the amino acid sequences. The argument has been considered but has not been found persuasive because the argument does not appear to be relevant to the instant rejection because the claims are not drawn to nucleic acids encoding SEQ ID NO:2, but rather are drawn to identifying nucleic acids encoding SEQ ID NO:2 that are mutated.

The arguments have been consider and have not been found persuasive.

8. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is indefinite in the recitation of the phrase a "heterologous nucleic acid of claim 1". The claim is indefinite as there is no antecedent basis for the claim limitation in claim 1 from which claim 30 depends.

Claim Rejections - 35 USC 102

9. Claims 1, 3-5, 30, 32, 36, 37 are rejected under 35 USC 102(b) as anticipated by US Patent No. 4, 594,318, of record as evidenced by Guru et al (Mammalian Genome, 1999, 10:592-596, IDS item).

Guru et al teach that human Menl gene is located on Chr 11q13. The claims are drawn to an isolated or recombinant nucleic acid encoding menin wherein said nucleic acid encodes a protein comprising an amino acid sequence having at least 95% identity to SEQ ID NO:2 (claim 1), comprising SEQ ID NO:1 (claim 3), comprising SEQ ID NO:3 (claim 4), encodes SEQ ID NO:2 (claim 5), a transfected cell comprising a heterologous nucleic acid of claim 1 (claim 30), wherein the nucleic acid comprises SEQ ID NO:1 and SEQ ID NO:3 (claim 32), an expression cassette comprising the nucleic acid of claim 1 operably linked to a promoter (claim 36), further comprising an expression vector (claim 37). US Patent No. 4,594,318 teaches isolated human chromosome 11 which comprises SEQ ID NO:3 and therefore encodes SEQ ID NO:2, a transfected cell comprising said chromosome, CHO-KI, which as defined by the specification is an expression vector.

Some of Applicant's arguments drawn to the rejection of the claims under 1, 3-5, 30, 32, 36, 37 are relevant to the instant rejection.

Applicant argues that the analysis of the term "isolated discounts the complete definition of "isolated" provided in the specification. In the definition of "isolated" on page 10 it explicitly states that "in particular, an isolated MEN1 gene is separated from open reading frames which flank the gene and encode a protein other than the MEN1 gene product." Thus, the specification teaches that "isolated" in context of a genomic MEN1 nucleic acid refers to a sequence that is separated

from open reading frames that flank the gene and encode a different protein. Given that the prior art reference does not teach the gene separated from open reading frames that flank the gene, the prior art reference is not anticipatory. The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted. Although the specification defines MEN1 gene in this manner, the claims are not drawn to MEN1 gene and the chromosome meets the limitations of the claims. Further, it is noted that the claims are not drawn solely to "isolated" nucleic acids but are also drawn to 'recombinant nucleic acid". Given that all chromosomes are in some sense recombinant, the prior art reference meets the limitations of the claims. It is noted that amendment of the claims to claim an isolated MEN1 gene would obviate the instant grounds of rejection.

Applicant argues that SEQ 1 is a cDNA sequence and chromosome does not contain an isolated cDNA sequence. The argument has been considered but has not been found persuasive because once again, Applicant is not arguing limitations recited in the claims as currently constituted. Claim 3 in particular is not drawn to SEQ ID NO:1, but rather is drawn to an isolated or recombinant nucleic acid wherein the sequence "comprises the coding region of SEQ ID NO:1". It is clear that the genomic sequence comprises the sequence of SEQ ID NO:1. It is noted that amendment of the claims to claim "wherein the sequence comprises SEQ ID NO:1" would obviate the instant grounds of rejection drawn to claims 3 and 32.

Applicant argues that, as drawn to claims 36 and 37, that the CHO-K1 somatic cell hybrid line is not an expression cassette as defined by the specification. Applicant point to page 9, lines 12-20 wherein the specification teaches that an expression cassette refers to a recombinant expression system for

expressing a nucleic acid sequence of the invention. The argument has been considered but has not been found persuasive because a review of page 9, lines 12-20 reveals that the specification states that "The term "expression cassette" refers to any recombinant expression system for the purpose of expressing a nucleic acid sequence of the invention in vitro or in vivo, constitutively or inducibly, in any cell. including prokaryotic, yeast, fungal, plant, insect or mammalian cell." Since all cells are in fact "recombinant" since recombination is the natural state of a cell when reproducing, the somatic cell hybrid line CHO-K1 meets the limitation of "any recombinant expression system". Amendment of the claims to specify any of the disclosed, but unlimited limitations such as "vectors. that remain episomal or integrate into the host cell genome", recombinant expression cassettes which contain expression vectors that "drive only transient expression in a cell", recombinant, recombinant expression cassettes which contain "only the minimum elements needed for transcription of the recombinant nucleic acid" would obviate the instant grounds of rejection.

10. No claims are allowed.

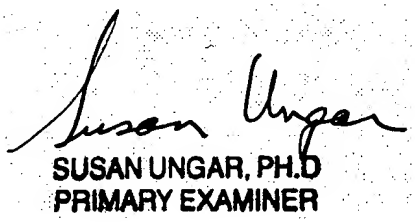
11. Claims 3, 4 and 32 are objected to as dependent upon a rejected base claim. Amendment of the claims to include all of the limitations of the intervening claims would render the claims allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898.. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susan Ungar
Primary Patent Examiner
December 11, 2006